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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/663,258	09/16/2003	Jose Engelmayer	H0-P02652US1	2875

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EXAMINER	
KAM, CHIH MIN	

ART UNIT	PAPER NUMBER
1656	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/663,258	ENGELMAYER ET AL.	
	Examiner	Art Unit	
	CHIH-MIN KAM	1656	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *01 April 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *15-51* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *15-51* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *16 September 2003* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Status of the Claims

1. Claims 15-51 are pending.

Applicants' Appeal Brief filed April 1, 2008 is acknowledged. Applicant's response has been fully considered. Since there is a new ground rejection in this Office Action, a non-final Office Action is issued. Therefore, claims 15-51 are examined.

Withdrawn Claim Rejections - 35 USC § 112

2. The previous rejection of claims 16-51 under 35 U. S. C. 112, first paragraph, regarding new matter, is withdrawn in view of applicants' response at pages 6-8 in the Appeal Brief filed April 1, 2008.

Withdrawn Claim Rejections -- 35 USC § 103

3. The previous rejection of claim 15 under 35 U.S.C. 103(a) as being unpatentable over Ando *et al.* (U. S. Patent 5,576,299) as evidenced by Engelmayer *et al.* (US 2004/0142037 A1), is withdrawn in view of applicants' response at pages 6-8 in the Appeal Brief filed April 1, 2008.

New Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

4. Claims 16-51 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant

art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a new matter rejection.

Claims 16-51 are directed to a method of treating a wound, other than burn wounds, oral wounds, ophthalmic wounds or gastric or duodenal ulcers, comprising the step of administering to a subject, other than by buccal administration, or administering topically, a therapeutically effective amount of a lactoferrin composition.

While the specification discloses the present invention is a method of treating a wound comprising the step of administering to a subject a lactoferrin composition in an amount sufficient to provide an improvement in the wound (paragraph [0017]), exemplary wounds that can be treated include skin wounds, bone wounds, internal wounds gastrointestinal wounds, oral wounds, ophthalmic wounds, surgical wounds, or any combination thereof (paragraph [0019]), and oral administration used includes oral, buccal, enteral or intragastric administration, the specification does not indicate that the use of a lactoferrin composition in the treatment of a wound including duodenal ulcers. Since the specification does not disclose duodenal ulcers as a wound to be treated with lactoferrin, the specification does not provide sufficient description for duodenal ulcers as an alternative wound to be treated as indicated in the claims. The lack of description of treating wounds of duodenal ulcers by administering a lactoferrin composition, and the lack of representative species as encompassed by the claims, applicants have failed to sufficiently describe the claimed invention, in such full, clear, concise terms that a skilled artisan would not recognize applicants were in possession of the claimed invention.

New Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

5. Claims 16-18, 21-23 and 26-51 are rejected under 35 U.S.C. 102(a) as anticipated by Boyko *et al.* (WO 02/03910, published January 17, 2000) based on the English translation provided by applicant.

Boyko *et al.* disclose a preparation of lactoferrin having antibacterial, antioxidant, detoxicating, anti-inflammatory, immunomodulating and anticarcinogenic effect is used for treating wound surface, where the preparation can be administered orally, intravenously, intracavitarily or intravesically, in the form of eye drops, inhalations or ointments, and the concentration of the active ingredient is 0.1-0.3% in a solution, the solution can be applied 2-3 times a day during a period of 3-15 days (pages 2-4; claims 16-18, 21-23 and 26-30). For example, in a patient diagnosed with third stage cervix uteri cancer, when applying complex radial therapy, occurrences of recititis (i.e., protitis, having red, sore, inflamed lining of rectum; see attached definition of the Dictionary) were observed in the patient. Applying rectal suppositories containing the lactoferrin preparation led to reducing the rectitis on the third day. A full course of radial therapy was administered continuously (page 9, first paragraph). Although Boyko *et al.* do not indicate administration of lactoferrin to the patient would supplement the local or systemic immune system, stimulate the production or inhibit of certain

cytokines or chemokines, or inhibit the production of matrix metalloproteinases, the reference teaches the same method steps (i.e., administration of lactoferrin) as the claimed method, thus, the lactoferrin would be expected to produce these effects (claims 31-51).

New Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

6. Claim 15 is rejected under 35 U.S.C. 103(a) as being unpatentable over Ando *et al.* (U. S. Patent 5,576,299, published November 19, 1996) in view of Ogunbiyi *et al.* (U.S. Patent 4,783,488).

Ando *et al.* disclose a formulation containing lactoferrin or transferrin is used for treating opportunistic infectious diseases under immunodeficient condition caused by Lentiviral infection (column 2, lines 10-21), e.g., granules containing human apolactoferrin (350 mg/day) were given to HIV positive patients with recurrent stomatitis and gingivitis once daily for 4 weeks, where the patients have aphthae or ulcers on the mucosa of the oral cavity and lip, and the inflammation in the oral cavity and pain was ameliorated after the treatment (Example 2) and feline immunodecificiency virus (FIV)-positive cats were treated with bovine native lactoferrin (20 mg/kg daily), which was dissolved in distilled water, and the solution was sprayed over ulcers and aphthae in the oral cavity, the treatment lasted 7 days to several months, and the appetite increased and the pain ameliorated after the lactoferrin treatment (Example 4). The reference

also teaches the pharmaceutical composition may contain the active compound (i.e., transferrin/lactoferrin) together with a solid or liquid pharmaceutically acceptable carrier, and suitable excipients such as sugar, gelatin, magnesium carbonate or magnesium stearate may be employed (column 4, line 21-column 5, line 3). However, Ando *et al.* do not specifically disclose the viscosity of gelatin.

Ogunbiyi *et al.* disclose the viscosity of gelatin solution at various gelatin concentrations (0.25% to 1.5%) and room temperature range from 5.06 CPS to 132.60 CPS (Example V).

At the time of invention was made, it would have been obvious to one of ordinary skill in the art that a lactoferrin composition comprising gelatin having a viscosity in the cited range at room temperature is used for treating wounds because gelatin is one of the polymers used as a liquid carrier in the lactoferrin composition for treating ulcers, and gelatin solution with the right viscosity can provide the desired wetting properties.

Response to Arguments

Applicants indicates Ando *et al.* disclose gelatin is used as a suitable excipient for the composition in the form of solutions, suspensions, tablets, pills, capsules, powders, sustained-release formulations and the like. However, the list does not indicate the compositional forms are granules (i.e., Example 2). Furthermore, Example 2 discloses the effects of lactoferrin to stimulate the immune system and thereby control opportunistic infections, it does not the step of contacting the wound with a pharmaceutical composition. While Example 4 discloses a procedure where bovine native lactoferrin is dissolved in distilled water and then the solution "sprayed over ulcers and aphthae [canker sores] in the oral cavity of cats with stomatitis and gingivitis caused by FIV and dental calculus, Example 4 is very clearly directed at treating two

of "[t]he most frequent opportunistic infections encountered in feline immunodeficiency virus (FIV) infected cats" stomatitis and gingivitis and not to a method of treating a wound. In this regard, Example 2 and 4 are indistinguishable in the target opportunistic infections against which they are directed. In addition, the composition used in Example 4 could not be more different than what claim 15 requires in that it is Lactoferrin in distilled water and lacks a polymer component altogether. Therefore, Ando *et al.* does not teach the claimed method. (pages 8-12 of the response).

Applicants' response has been considered, however, the arguments are not found persuasive because of the following reasons. While the list does not specifically indicate the compositional forms are granules (i.e., Example 2), it does disclose the composition is in the form of solutions, suspensions, tablets, pills, capsules, powders, sustained-release formulations and the like, which would include granules. Furthermore, in Example 2, granules containing lactoferrin were given to the patients with aphthae or ulcers on the mucosa of oral cavity and lip, thus these granules, which are administered orally, are contacted with wounds. Example 4 shows the solution of bovine lactoferrin is sprayed over ulcers and aphthae in the oral cavity of cats with stomatitis and gingivitis, which has the same method step (i.e., contacting wounds with the composition) as the claimed method. While the Examples 2 and 4 do not indicate the composition contains the polymer, the reference does suggest a suitable pharmaceutical excipient such as gelatin can be added to the composition for proper administration (column 4, line 53-column 5, line 3). Therefore, one of ordinary skill in the art would conclude that a lactoferrin composition can comprise a suitable pharmaceutical excipient for a proper administration.

7. Claims 16, 17, 21-23, 26, 28 and 30-47 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kruzel *et al.* (US Patent 6,066,469, published on may 23, 2000).

Kruzel *et al.* disclose treating accidental scratches and burns (column 6, lines 14-16) by topical administration of lactoferrin in an ointment, cream or other topical vehicle twice daily in an amount of 50-100 mg per dose for a period of time of three to four weeks (column 5, line 61-column 6, line 39; column 7, lines 44-53; claims 16-17, 21-23, 26, 28 and 30). Although Kruzel *et al.* do not indicate administration of lactoferrin to the patient would supplement the local immune system, stimulate the production or inhibit of certain cytokines or chemokines, or inhibit the production of matrix metalloproteinases, the reference teaches the same method steps (i.e., administration of lactoferrin) as the claimed method, thus at the time of invention was made, it would have been obvious to one of ordinary skill in the art that the lactoferrin composition would produce these effects (claims 31-47).

Maintained Claim Rejections-Obviousness Type Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

8. Claims 15-51 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-16 of U. S. Patent 7,323,443 (previous U.S.

Application No. 10/733,621). Although the conflicting claims are not identical, they are not patentably distinct from each other because claims 15-51 in the instant application disclose a method of treating a wound (or a wound other than burn wounds, oral wounds, ophthalmic wounds or gastric or duodenal ulcers), or enhancing the local or systemic immune system in a subject suffering from a wound by administering to the subject an effective amount of a lactoferrin composition comprising a lactoferrin, or a lactoferrin and a pharmaceutically acceptable polymer having a viscosity in the range of about 1 to 12,000,000 cp at room temperature; and the specification discloses a lactoferrin composition can be a composition having an N-terminal lactoferrin variant such as the variant that lacks N-terminal glycine [0010]. This is an obvious variation in view of claims 1-16 in the patent which disclose a method of treating a subject suffering from pain comprising the step of administering to the subject an effective amount of a lactoferrin composition comprising an N-terminal lactoferrin variant, wherein the pain is associated with recovery from surgery, and the N-terminal lactoferrin variant has a deletion or substitution or combination of 1 to 16 N-terminal amino acid residues and retains the same biological function as the full length lactoferrin; and the specification discloses the composition comprising a lactoferrin and a pharmaceutically acceptable carrier which can be a gel composition comprising Carbopol. Both the claims of instant application and the claims of the patent are directed to a method of treating wound or a patient having a pain from surgery by administering a lactoferrin composition (i.e., the same method steps), where a patient having a pain from surgery would have a wound. Thus, claims 15-51 in present application and claims 1-16 in the patent are obvious variations of a method of treating wound or pain from surgery (a wound) by administering a lactoferrin composition.

Response to Arguments

Applicants indicate the Examiner has not provided any reasoning why a person of ordinary skill has recognized the instantly claimed invention obvious over the claims of the commonly owned application (10/733,621). The Examiner has only provided a summary of the two claimed inventions followed by a conclusory statement combining the claimed elements of of the two applications, with no specific recitation of why the claims would obvious. Applicants assert that the Examiner has not met the burden required for making a proper double patenting rejection. Thus, Applicants request reversal of the rejection (pages 14-15 of the response).

Applicants' response has been considered, however, the arguments are not found persuasive because of the following reasons. While the instant application claims a method of treating wounds with a lactoferrin composition, and the patent claims a method of treating a subject suffering from pain with a lactoferrin composition comprising an N-terminal variant, where the pain is associated with recovery from surgery (having a wound), the two methods have the same method step of administering a lactoferrin composition (e.g., an N-terminal variant) to a patient having a wound. Therefore, the two claimed methods are not patentably distinct from each other, and the rejection under the judicially created doctrine of obviousness-type double patenting is maintained.

9. Claims 16-22, 26-30 and 50-51 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1, 7, 14, 17-19, 26-32 and 38-40 of copending Application No. 10/728,521 (based on the amended claims filed September 26, 2006). Although the conflicting claims are not identical, they are not patentably distinct from each other because claims 16-22, 26-30 and 50-51 disclose a method of treating a

wound other than ophthalmic wounds, or enhancing the local or systemic immune system in a subject suffering from a wound by administering to the subject an effective amount of a lactoferrin composition; and the specification indicates a lactoferrin composition can have an N-terminal lactoferrin variant such as N-terminal glycine deleted or substituted or a deletion, substitution, or combination thereof, of from 1 to 16 N-terminal amino acid residues and the N-terminal lactoferrin variant retains the same biological function as full length lactoferrin (paragraphs [0009] and [0048]), and the lactoferrin composition can decrease bacterial infection of the wound (paragraphs [0102]). This is an obvious variation in view of claims 1, 7, 14, 17-19, 26-32 and 38-40 in the copending application which disclose a method of treating bacteremia or sepsis, enhancing a mucosal response in the gastrointestinal tract or decreasing mortality of a subject having bacteremia, comprising the step of administering orally to a subject an effective amount of a lactoferrin composition comprising at least 1% to at least 50% w/w of an N-terminal lactoferrin variant to provide an improvement in the bacteremia of said subject, wherein the N-terminal lactoferrin variant has a deletion, substitution, or combination thereof, of from 1 to 16 N-terminal amino acid residues and wherein the N-terminal lactoferrin variant retains the same biological function as full length lactoferrin; and the specification indicates sepsis or bacteremia may originate anywhere in the body such as surgical wounds or decubitus ulcers (paragraphs [0003] and [0082]). Both the claims of instant application and the claims of the copending application are directed to a method of treating bacteremia or sepsis, or treating wounds such as wounds causing bacteremia or sepsis by administering a lactoferrin composition comprising an N-terminal lactoferrin variant. Thus, claims 16-22, 26-30 and 50-51 in present application and claims 1, 7, 14, 17-19, 26-32 and 38-40 in the copending application are obvious variations of a

method of treating bacteremia or sepsis, or wounds causing bacteremia or sepsis by administering a lactoferrin composition comprising an N-terminal lactoferrin variant.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Response to Arguments

Applicants indicate the Examiner has not provided any reasoning why a person of ordinary skill have recognized the instantly claimed invention obvious over the claims of the commonly owned application (10/728,521). The Examiner has only provided a summary of the two claimed inventions followed by a conclusory statement combining the claimed elements of of the two applications, with no specific recitation of why the claims would obvious. Applicants assert that the Examiner has not met the burden required for making a proper double patenting rejection. Thus, Applicants request reversal of the rejection (pages 12-14 of the response).

Applicants' response has been considered, however, the arguments are not found persuasive because of the following reasons. While the instant application claims a method of treating wounds with a lactoferrin composition, and the copending application claims a method of treating a subject having bacteremia with a lactoferrin composition comprising an N-terminal variant, the two methods have the same method step of administering a lactoferrin composition (e.g., an N-terminal variant) to a patient having a wound or bacteremia, where the bacteremia may originate anywhere in the body such as surgical wounds or decubitus ulcers. Therefore, the two claimed methods are not patentably distinct from each other, and the rejection under the judicially created doctrine of obviousness-type double patenting is maintained.

Conclusion

10. No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Chih-Min Kam whose telephone number is (571) 272-0948. The examiner can normally be reached on 8.00-4:30, Mon-Fri.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Kathleen Bragdon can be reached at 571-272-0931. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/Chih-Min Kam/
Primary Examiner, Art Unit 1656

CMK
June 19, 2008